NKY - 0014

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing (*day/month/year*)	23 JUN 2004

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
033388-531	

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US03/00380	08 January 2003 (08.01.2003)	09 January 2002 (09.01.2002)

Applicant

ELAN PHARMACEUTICALS

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450	Valerie Bell-Harris for Richard Schnizer, Ph. D
Facsimile No. (703) 305-3230	Telephone No. 571/272-1600

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 033388-531	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/00380	International filing date *(day/month/year)* 08 January 2003 (08.01.2003)	Priority date *(day/month/year)* 09 January 2002 (09.01.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 15/88; A01N 43/04 and US Cl.: 424/450; 514/4; 435/458		
Applicant ELAN PHARMACEUTICALS		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30 July 2003 (30.07.2003)	16 June 2004 (16.06.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Valerie Bell-Harris for Richard Schnizer, Ph. D Telephone No. 571/272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRE[redacted]NARY EXAMINATION REPORT

Intern[redacted]nal application No.
PCT/US03/[redacted]

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-38 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 39-69, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-9, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.
PCT/US03/00380

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 143, 145

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 143, 145 are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 143 and 145

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.
PCT/US03[redacted]0

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Inventive Step (IS)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Industrial Applicability (IA)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-34 and 38-73, 147, 149, 153-167 lack novelty under PCT Article 33(2) as being anticipated by Eppstein et al (US Patent 4897335).

Claims 1-34 and 38-73 are directed to liposomes comprising nucleic acids. The liposomes are made by a particular process which has been given no patentable weight in the determination as to whether the claimed products are novel. Eppstein teaches a variety of liposomes comprising nucleic acids. The liposomes may comprise varying amounts of the fusogenic lipid DOPE. The nucleic acid may be plasmid DNA, or an antisense RNA oligonucleotide. The liposomes may comprise a variety of lipids including distearoyl phosphatidylcholine and cholesterol. Eppstein also teaches intravenous delivery to humans. See entire document.

Claims 1-6, 8-17, 25, 29-31, 33, 34, 38-79, 87, 90-104, 142, 144, and 153-167 lack novelty under PCT Article 33(2) as being anticipated by Papahadjopolous et al (US Patent 4235871).
Claims 1-6, 8-17, 25, 29-31, 33, 34 are directed to liposomes comprising nucleic acids. The liposomes are made by a particular process which has been given no patentable weight in the determination as to whether the claimed products are novel. Papahadjopolous teaches a variety of liposomes comprising nucleic acids. The liposomes may comprise varying amounts of the fusogenic lipid DOPE. The nucleic acid may be plasmid DNA, or an RNA. The liposomes may comprise a variety of lipids including distearoyl phosphatidylcholine and cholesterol. See entire document.
Papahadjopolous teaches a method of making liposomes by combining lipids and nucleic acids in an organic solvent to form an emulsion, and thereafter forming a gel in which are subsequently formed liposomes. See entire document, especially e.g. claim 1.

Claims 7, 18-24, 26-28, 32, 80-86, 88, 89, 105-107, 111-141, 146-148, 150, 151, 152, and 168 lack an inventive step under PCT Article 33(3) as being obvious over Papahadjopolous et al (US Patent 4235871), in view of Eppstein et al (US Patent 4897335).
The teachings of Papahadjopolous are described above. Presently claimed limitations concerning the amount of lipids in gels or liposomes, the identity of organic solvents used in liposome formation, the order in which components are added to mixtures, the size of plasmid DNAs, and the identity of liposome forming lipids are taken to be parameters that are routinely optimized by those of ordinary skill in the art, particularly in view of the teachings of Eppstein who discloses a variety of lipids, solvents, and nucleic acids. Eppstein also teaches the use of these liposomes to deliver bioactive substances such as nucleic acids in vivo by intravenous administration. See entire document.

Claims 35-37 and 108-110 lack an inventive step under PCT Article 33(3) as being obvious over Papahadjopolous et al (US Patent 4235871) in view of Meers et al (US Patent 6,120,797).
The teachings of Papahadjopolous are described above. Papahadjopolous does not teach N-acyl phosphatidylethanolamines.
Meers teaches a N-dodecanoyl dioleoyl phosphatidylethanolamine for use in liposome formation.
It would have been obvious to use the lipid of Meers in the liposomes of Paphadjopolous because Meers teaches that it promotes membrane fusion. See e.g. column 1, lines 48-60.

---------- NEW CITATIONS ----------

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V.1. Reasoned Statements:
The opinion as to Novelty was positive (Yes)with respect to claims 35-37, 80-86, 88, 89, 105-142, 145, 146, 148, 150-152, and 168
The opinion as to Novelty was negative (No) with respect to claims 1-34, 38-79, 87, 90-104, 142, 144, 147, 149, 153-167
The opinion as to Inventive Step was positive (Yes)with respect to claims NONE
The opinion as to Inventive Step was negative(NO) with respect to claims 1-142, 144, 146-168
The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-142, 144, 146-168
The opinion as to Industrial Applicability was negative(NO) with respect to claims NONE